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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/532,374	04/21/2005	Jay A Berzofsky	4239-67016-02	4276

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EXAMINER	
HUFF, SHEELA JITENDRA	
ART UNIT	**PAPER NUMBER**
1643	

MAIL DATE	DELIVERY MODE
11/08/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/532,374	BERZOFSKY ET AL.	
	Examiner	Art Unit	
	Sheela J. Huff	1643	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *10 October 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,6-11,13-18,21,26-28,32-34 and 38-45* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1, 6-11, 13-18, 21, 26-28, 32-34 and 38-45* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Response to Amendment

The amendment filed on 10/10/07 has been considered. Applicant's arguments are deemed to be persuasive-in-part.

Claims 1, 6-11, 13-18, 21, 26-28, 32-34 and 38-45 are pending.

The objection of claim 12 is withdrawn in view of its cancellation.

The double patenting issue of claim 25 is withdrawn in view of its cancellation.

All art rejections are withdrawn in favor of new ones.

Response to Arguments

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 26-28 and remain rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The reasons for the rejection are set forth in the paper mailed 6/8/07. Note Items a, b and d have been removed from this rejection.

Applicant argues that the activity is the increased tumor immunosurveillance. The claim, as written, does not show this correlation.

Claims 39-45 remain rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. The reasons for the rejection are set forth in the paper mailed 6/8/07.

Applicant argues that the specification sets out methods for identifying agents which can inhibit tumor recurrence and that such experimentation is routine in the art. The Examiner carefully considered the specification prior to making this rejection. Applicant has not responded to the issues in the rejection.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1, 6-9, 11, 13-15, 21, 26-28, 32-34 and 38 are rejected under 35 U.S.C. 103(a) as being unpatentable over Dasch et al US 6090383 in view of Barbera-Guillem US 6224866, Rosenblum US 2005/0214307 (filed 3/17/95) and Zavada et al US 6297041.

Dasch et al discloses and claims methods for treating tumor cells by administering monoclonal antibodies reactive to TGF-beta to suppress the immunosuppressive effects of TGF-beta and to permit generation of an immune response against the tumor and this results in tumor regression (col. 2, lines 28-32 and col. 5, lines 54-58). Tumors include sarcomas, melanomas and carcinomas (col. 2, lines 8-10 and col. 5, lines 48-50). The preferred monoclonal antibody is Mab 1D11.16 (which is the same one used by applicant, col. 5, lines 18+). The antibody neutralizes the biological activity of TGF-beta an prevents binding of antigen to cell surface receptors (col. 5, lines 58-60). The biological activities of TGF-beta include suppressing

the proliferation of T and B cells and that the Mab of the invention blocks the TGF-B's immunosuppressive effects. (col. 1, lines 20-40 and col. 5, lines 48+). The antibodies are can be administered by intraveneous or peritoneal perfusion or by bolus injection into the muscle or subcutaneous tissue (col. 6, lines 26-30) to patients (col. 6, lines 5-9).

This reference does not specifically discuss the treatment of tumor recurrence.

It is known in the art that compounds that treat tumors can also be used to treat tumor recurrence. For example, Barbera-Guillem discloses that one skilled in art would readily recognize that the same procedure used for treating a cancer would also be used for the treatment of recurrence of the same cancer (col. 23, lines 20-25). It is also that the reference discloses antibody therapy, which is the same type of therapy used by applicant. Rosenblum discloses that the same antibody used in treatment of tumors is used in the treatment of tumor recurrence (paragraph [0043]). Zavada et al discloses the same compounds (which include polypeptides and antibodies) can be used for treatment and treatment of recurrence (col. 10, line 50 to col. 11, line 10). Thus, the use of the same antibody in treatment of tumors is also used in the treatment of recurrent tumors.

Because it is well known in the art to use the same antibody used in treatment of a tumor as in the treatment of tumor recurrence, it would have been obvious to one of ordinary skill in the art at the time of applicant's invention to use the antibody of the primary reference in the treatment of tumor recurrence. Furthermore, since both applicant and the primary reference use the exact same antibody and since the

antibody has been shown in the primary reference to block the TGF-B's immunosuppressive effects (which include suppressing the proliferation of T and B cells and NK cells) and result in tumor destruction, the property of increased tumor immunosurveillance is an expected property of the antibody in the reference.

Response to applicant's arguments to the extent that they read on the instant rejection

Applicant argues that Dasch et al disclose the treatment of an existing tumor not a tumor that has recurred at the same site and is a variant form of the original tumor. Applicant is arguing limitations (ie variant form) that is not found in claims or specification. Applicant is cautioned against the addition of new matter. Additionally, the secondary references clearly show that it is known in the art to use the same compound to treat the original tumor and a recurring tumor.

Claims 1, 6-11, 13-15, 21, 26-28, 32-34 and 38 are rejected under 35 U.S.C. 103(a) as being unpatentable over Dasch et al US 6090383 in view of Barbera-Guillem US 6224866, Rosenblum US 2005/0214307 (filed 3/17/95) and Zavada et al US 6297041 and Suthanthiran et al US 2004-0197333 (filed 2/10/00).

Dasch et al, Barbera-Guillem, Rosenblum and Zavada et al have been discussed above.

The only difference between the instant invention and the combination of the references is the specific mention of the difference types of cancers.

Suthanthiran et al discloses the use of TGF-beta antagonists, which includes monoclonal antibodies (abstract, [0024]) to treat a variety of different cancers known to be associated with TGF-beta. These include cancers of the breast, lung, small intestine (reads on gastrointestinal), solon, kidney, ovary, prostate, brain, pancreas, skin, bone, uterus, testicles, cervix and liver ([0019).

Therefore, in view of the fact that is it known that TGF-beta antagonists, including monoclonal antibodies, to treat include cancers of the breast, lung, small intestine (reads on gastrointestinal), solon, kidney, ovary, prostate, brain, pancreas, skin, bone, uterus, testicles, cervix and liver and in view of the fact that mab 1D11.16 inhibits binding of TGF-beta to its receptor and inhibits its function (as disclosed in Dasch et al) (in other words 1D11.16 is behaving as an antagonist), it would have been obvious to one of ordinary skill in the art at the time of applicant's invention to use 1D11.16 to treat cancers of the breast, lung, small intestine (reads on gastrointestinal), solon, kidney, ovary, prostate, brain, pancreas, skin, bone, uterus, testicles, cervix and liver.

Claims 1, 6-9, 11, 13-18, 21, 26-28, 32-34 and 38 are rejected under 35 U.S.C. 103(a) as being unpatentable over Dasch et al US 6090383 in view of Barbera-Guillem US 6224866, Rosenblum US 2005/0214307 (filed 3/17/95) and Zavada et al US 6297041 and Terabe et al Nature Immunology vol. 1 p. 515 (12/00).

Dasch et al, Barbera-Guillem, Rosenblum and Zavada et al have been discussed above. Dasch et al also disclose the use of the mab in an assay to monitor tumor mass

(col. 6, lines 44-61). Thus, this reference is also disclosing methods for monitoring tumor progression (reads on tumor immunosurveillance).

The only difference between the instant invention and the reference is the specific mention of the specific assays used for tumor immunosurveillance.

Terabe et al show that the assays of claims 16-18 are known in the art (see page 520, first column) and are used in tumor immunosurveillance (see entire reference).

Thus, in view of the known use of the assays for tumor immunosurveillance and in view of the fact that the primary reference calls for monitoring tumor progression, it would have been obvious to one of ordinary skill in the art at the time of applicant's invention to use these assays to monitor tumor progression.

Conclusion

The prior art made of record and not relied upon is considered pertinent to applicant's disclosure. Dasch et al J. Immunol. Vol. 142 p. 1536 (1989).

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Sheela J. Huff whose telephone number is 571-272-0834. The examiner can normally be reached on Tuesday and Thursday from 5:30am to 1:30pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Larry Helms can be reached on 571-272-0832. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Sheela J Huff
Primary Examiner
Art Unit 1643

sjh